UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

005234

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUN 30 1986

MEMORANDUM

SUBJECT: Preliminary Review of Combined Toxicity and Oncogenicity Study in Rats on 2,4-Dichlorophenoxy-acetic acid.

FROM: Marcia van Gemert, Ph.D. M. van Gemert 6.30.86
Head, Section III
Toxicology Branch, HED (TS-769C)

TO: Lois Rossi
Special Review Branch
Registration Division (TS-767C)

THRU: Theodore M. Farber, Ph.D. Theodore M. Farber 6/30/86
Chief
Toxicology Branch/HED (TS-769C)

Compound: 2,4-Dichlorophenoxyacetic acid

Tox. Chem. No.: 315

Registrant: Industry Task Force on 2,4-D Research Data

Accession No.: 030001

Action Requested:

Review the toxicology/oncogenicity study submitted on 2,4-dichlorophenoxyacetic acid, possible 6(a)(2) action.

Conclusions:

The administration of 2,4-D appears to produce increased numbers of astrocytomas in brains of male rats at 45 mg/kg/day and is suggestive of a carcinogenic effect. The final determination of oncogenicity will come after a joint review with the Canadian Health Protection Branch, an evaluation of the brain and spinal cord slides by EPA officials, and presentation of the weight of evidence before the EPA Peer Review Committee.

The Task Force that submitted the study to EPA is presently re-evaluating the brain slides by an independent pathologist to confirm the diagnosis of astrocytoma, and will

submit a report of this re-evaluation in July, 1986.

The task force should be requested to submit summary tables for the urinalysis data which were missing from the text of the study. They should also be asked to re-tabulate and submit clearer summary tables of the non-neoplastic and neoplastic lesions. Examples of summary incidence tables are appended to this memo for clarification. The Task Force should also be requested to submit all brain and spinal cord slides of control and experimental animals. Based on the non-neoplastic lesions seen in the kidney, (see DER)

the NOEL = 1 mg/kg/day and the LEL = 5 mg/kg/day.

Core Classification: Will be assigned pending receipt of the requested data.

Reviewed by: Marcia Van Gemert, Ph.D. M. Van Gemert 6.30.86
Section 3, Tox. Branch (TS-769C) Section Head
Secondary reviewer: Theodore M. Farber, Ph.D. Theodore M. Farber
Chief, Tox. Branch (TS-769)

DATA EVALUATION REPORT

STUDY TYPE: Combined toxicity & oncogenicity TOX. CHEM. No.: 315

ACCESSION NUMBER: 263112-263114 MRID No.:

TEST MATERIAL: Dichlorophenoxyacetic acid

SYNONYMS: 2,4-D

STUDY NUMBER(S): 2184-103

SPONSOR: Industry Task Force on 2,4-D Research Data

TESTING FACILITY: Hazleton Labs, 9200 Leesburg Turnpike
Vienna, Virginia 22180

TITLE OF REPORT: Combined Toxicity and Oncogenicity Study in Rats
2,4-Dichlorophenoxyacetic acid, final report

AUTHOR(S): D.G. Serota, Ph.D. - Study Director

REPORT ISSUED: May 29, 1986

CONCLUSIONS: Increased astrocytomas in male rats at 45 mg/kg
NOEL = 1 mg/kg/day
LEL = 5 mg/kg/day based on kidney effects
Classification: Will be assigned pending receipt of the requested information.

A. MATERIALS:

1. Test compound: 2,4-D, Description of test material is on appended pg.1 Purity 97.5%, contaminants: list in CBI appendix

2. Test animals: Species: rats, Strain: CDF(F344)/CRL-BR, Age: 7 wks.
Weight: 125.8-158.3, 94.4-118.5 Source: Charles River Breeding Labs Kingston, New York

B. STUDY DESIGN:

1. Animal assignment - 600 animals were assigned to the following test groups:

TABLE 1

Test Group	Dose in diet mg/kg/day	Main Study 104 wks. male	female	Interim Sac. 53 weeks male	female
1 Cont.	0	60	60	10	10
2 Low (LDT)	1	60	60	10	10
3 Mid-1 (MDT)	5	60	60	10	10
4 Mid-2	15	60	60	10	10
5 High	45	60	60	10	10

2. Diet preparation - Diet was premixed in 200 gms of basal diet and prepared weekly for 1st 14 weeks biweekly through week 18 then every 4th week thereafter and stored at room temperature. Samples of treated food were analyzed for stability and concentrations of 2,4-D in diet for weeks 1, 2, 3, 4, 17, 30, 43, 56, 69, 82, 95.

Results - Analysis of the diet indicated 2,4-D was stable in the diet for at least one month.

TABLE 2

Analysis of 2,4-D Concentrations

Groups	Percentage of Target Range		Mean & S.D.
	Low	High	
2	84.6	120.3	101.96 ± 9.54
3	82.1	125.3	100.6 ± 9.2
4	80.8	122.2	97.8 ± 8.7
5	81.9	113.4	98.1 ± 7.2

3. Animals received food (Diet + 2,4-D) and water ad libitum.

4. Statistics - The following procedures were utilized in analyzing the numerical data: (See appended pgs. 2&3).

5. Quality assurance was in compliance with EPA GLP regulations.

C. METHODS AND RESULTS:

1. Observations - Animals were inspected twice/day for signs of toxicity and mortality.

Detailed physical exams for physical appearance, behavior tissue mass palpation and signs of abdominal distention were made weekly for 1st 14 weeks and biweekly thereafter.

Results - Toxicity - no treatment related effects on mortality (survival) were noted. (See appended pages 4 & 5).

TABLE 3

Mortality and (Percent Survival) at Month[a]

		6	12	18	24
			Males		
Group	1	1 (98)	1 (98)	2 (95)	18 (64)
	2	0 (100)	0 (100)	2 (95)	7 (85)
	3	0 (100)	0 (100)	0 (100)	2 (96)
	4	1 (98)	2 (97)	3 (94)	8 (84)
	5	0 (100)	0 (100)	0 (100)	12 (76)
			Females		
	1	1 (98)	2 (97)	4 (92)	10 (80)
	2	0 (100)	0 (100)	1 (98)	13 (74)
	3	0 (100)	0 (100)	0 (100)	2 (96)
	4	1 (98)	2 (97)	3 (94)	8 (84)
	5	0 (100)	0 (100)	0 (100)	12 (76)

a. Percent survival based on 60, 60, 50 and 50 rats/sex/group at 6, 12, 18 and 24 months, respectively.

2. Body Weight - Animals were weighed at initiation of the experiment and weekly for 1-14 weeks then biweekly for remainder of experiment.

Results - Statistical analysis of absolute body weight at week 52, body weight changes at weeks 0-52 and 0-104 and growth rate data showed significantly decreased mean values for group 5 females. (see appended pages 6 & 7 for cumulative body weight gain.)

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TABLE 4

MEAN CUMULATIVE BODY WEIGHT GAIN

	0-52 Weeks females			males			0-104 weeks males		females		
	N	Mean	S.D.	N	Mean	S.D.	N	Mean	N	Mean	S.D.
1	58	113.4	11.57	59	229.6	18.30	32	216.8	40	145.6	14.87
2	60	114.1	8.61	60	225.4	17.33	43	211.2	37	142.9	26.0
3	60	116.7	11.77	60	227.1	19.28	48	214.5	38	141.0	22.07
4	60	113.5	12.43	58	232.3	16.88	42	213.9	38	144.8	17.22
5	60	105.2*	11.31	59	227.9	14.05	37	206.5	36	132.8*	17.14

* Significantly different from control $p \leq 0.05$

3. Food consumption and compound intake - Consumption was determined and mean daily diet consumption was calculated. Food consumption was measured weekly for first 14 weeks and then biweekly for the remainder of the experiment.

Results - Food consumption - mean values for Group 5 females were significantly lower than control values at weeks 1 - 52. Also the mean value for Group 2 females was significantly higher than the mean value for Group 1 females at this time interval.

TABLE 5

MEAN TOTAL FOOD CONSUMPTION -Females

	0-52 weeks N	Mean	SD	0-104 weeks N	Mean	SD
1	58	3114.9	169.52	40	5861.8	289.84
2	57	3198.9*	171.65	34	5989.4	313.94
3	56	3174.9	164.39	35	6022.7	319.78
4	60	3115.7	166.14	38	5816.9	304.19
5	60	3038.6*	140.29	35	5751.4	291.19

*Significantly different from control $p \leq 0.05$

4. Ophthalmalogical examinations were performed at end of 52 weeks and at 104 weeks all animals.

Results - Ophthalmic exam revealed no ocular toxicity that could be associated with 2,4-D administration at any dose.

5. Blood was collected before treatment and at 26, 52 and 78 weeks for hematology and clinical analysis from 10 animals/sex/group. Clinical analysis was collected on all animals surviving to termination of study. The checked (X) parameters were examined.

a. Hematology -

X		X	
X	Hematocrit (HCT)*	X	Total plasma protein (TP)
X	Hemoglobin (HGB)*	X	Leukocyte differential count
X	Total leukocyte count (WBC)*		Mean corpuscular HGB (MCH)
X	Erythrocyte count (RBC)*		Mean corpuscular HGB conc. (MCHC)
X	Platelet count*		Mean corpuscular volume (MCV)
X	Reticulocyte count		

Results -

No treatment-related results on the hematological parameters measured were apparent.

b. Clinical Chemistry

X		X	
	Electrolytes:		Other
X	Calcium*	X	Albumin*
	Chloride*		Blood creatinine*
	Magnesium*	X	Blood urea nitrogen*
	Phosphorous*		Cholesterol*
X	Potassium*	X	Globulins
X	Sodium*	X	Glucose*
	Enzymes	X	Total Bilirubin*
X	Alkaline phosphatase		Triglycerides
	Cholinesterase	X	Albumin/globulin ratio
	Creatinine phosphokinase*	X	Thyroxine
X	Lactic acid dehydrogenase	X	Total protein
X	Serum alanine aminotransferase (also SGPT)*		
X	Serum aspartate aminotransferase (also SGOT)*		

Results -

1. there was a slight ($p \leq .05$) increase in the albumin and a slight decrease ($p \leq 0.05$) in globulin at week 105 in males, increasing the A/G ratio at both 79 and 105 weeks ($p < 0.05$). (see appended pages 8 & 9)

2. There was slight ($p \leq 0.05$) increase in serum alanine aminotransferase in males and females at week 105 in Group 5. (see appended page 10)

3. T_4 was slightly depressed ($p \leq 0.05$) at 105 weeks in group 5 females. (see appended page 11)

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6. Urinalysis - Urine was collected from 10 rats/sex/group at initiation and following weeks 26, 52, and 78 weeks of treatment. The CHECKED (X) parameters were examined.

X		X	
	Appearance*	X	Glucose*
	Volume*	X	Ketones*
X	Specific gravity*	X	Bilirubin*
X	pH		Blood*
	Sediment (microscopic)*		Nitrate
X	Protein*	X	Urobilinogen

Results - Tables on mean values for urinalysis were missing from the text.
There appears to be a decrease in urinary protein at the highest dose level. Summary tables will have to be generated before this can be verified.

7. Sacrifice and Pathology -
All animals that died and that were sacrificed on schedule were subject to gross pathological examination and the CHECKED (X) tissues were collected for histological examination. The (XX) organs in addition were weighed.

Digestive system		Cardiovasc./Hemat.		Neurologic	
	Tongue		Aorta*	XX	Brain*
X	Salivary glands*	XX	Heart*	X	Periph. nerve* (sciatic)
X	Esophagus*	X	Bone marrow*	X	Spinal cord
X	Stomach*	X	Lymph nodes*	XX	Pituitary*
X	Duodenum*	X	Spleen*	X	Eyes (optic n.)*
X	Jejunum*	X	Thymus*	Glandular	
X	Ileum*	Urogenital		XX	Adrenals*
X	Cecum*	XX	Kidneys*		Lacrimal gland
X	Colon*	X	Urinary bladder*		Mammary gland*
	Rectum*	XX	Testes*	XX	Parathyroids*
XX	Liver*	XX	Epididymides	XX	Thyroids*
	Gall bladder*	X	Prostate	Other	
X	Pancreas*		Seminal vesicle	X	Bone*(sternum with marrow)
Respiratory		XX	Ovaries	X	Skeletal muscle*
X	Trachea*	X	Uterus*	X	Skin
X	Lung*			X	All gross lesions and masses

Summaries of the pathology protocols for the 52-week sacrifice, unscheduled deaths, and the terminal sacrifices are appended on pages 12 and 13. The study states that "brain" sections (including at least one section of the forebrain, mid brain and hind brain) were examined microscopically by the study pathologist and then read blind by a second pathologist. Following these examinations remaining fixed brain tissue from each animal

was processed and evaluated microscopically by the study pathologist. These observations were incorporated into the original findings to yield a composite incidence from both evaluations.

I called Dr. David Sorota of Hazelton Laboratories, the Study Director, and asked specifically how the brain was sectioned. He said originally only one section from fore, mid and hind brain was examined. But after finding some astrocytomas, they then sectioned all available brain tissue from each rat. We are in the process of formally writing to the Task Force for written confirmation of this statement.

Results -

a. Organ Weight

Interim sacrifice

Kidney weight parameters measured, eg. absolute organ weight, organ-to-body weight, and organ-to-brain weight were significantly elevated in the group 5 males. Females showed a slight increase in kidney weight parameters no other significant organ weight changes were noted. (see table 6 for details.)

TABLE 6

ORGAN WEIGHTS 52 WEEK SACRIFICE

		Absol. Wts		organ-to body wts.		organ-to-brain wts.	
Kidney Male	#	Mean	SD	Mean	SD	Mean	SD
1	10	2.44	.17	.693	.043	1.225	.061
2	10	2.43	.11	.684	.022	1.214	.041
3	10	2.46	.26	.698	.050	1.225	.107
4	10	2.61	.12	.738	.037	1.295	.053
5	10	2.66*	.15	.780*	.057	1.344*	.091
Kidney Female							
1	10	1.57	.10	.805	.090	0.876	.046
2	10	1.62	.13	.802	.067	0.901	.055
3	10	1.56	.10	.785	.052	0.873	.069
4	10	1.62	.05	.784	.036	0.892	.034
5	10	1.60*	.09	.829*	.037	0.884	.048

*Significantly different from controls $p \leq 0.05$

Terminal Sacrifice

At 105 weeks there was an increase in kidney weight parameters in groups 4 and 5 with statistical

significance in the females ($p \leq 0.05$) in group 5 in all parameters. (Table 7) The increases in kidney weight values appear to be treatment-related. There appeared to be a dose-related increase at 104 weeks in all male thyroid/parathyroid parameters with statistical significace generally in groups 4 and 5. In female there appeared to be a trend of increased values in groups 3, 4, and 5 with group 4 having statistical significance. This appears to be a treatment-related effect. The other organ weights that were significantly different from control were noted in group 5. These organs include liver and thyroids/parathyroids in males, pituitary, brain with brain stem, and ovaries in females. Those changes in the pituitary, liver and ovaries appear treatment-related.

TABLE 7

ORGAN WEIGHTS 104 WEEK SACRIFICE

		Absolute Organ wt.		Organ-to-Body wt.		Organ-to-Brain wt.	
LIVER Male	N	Mean	SD	Mean	SD	Mean	SD
1	32	10.02	2.02	2.996	.664	4.846	.962
2	43	9.66	1.14	2.956	.390	4.702	.560
3	47	9.94	1.69	2.992	.538	4.827	.814
4	41	9.41	1.25	2.837	.337	4.609	.592
5	36	8.82	1.29	2.730	.543	4.277*	.658
LIVER Female							
1	40	7.14	1.35	3.072	.638	3.811	.658
2	37	7.16	0.95	3.102	.487	3.812	.483
3	37	7.07	1.20	3.099	.509	3.799	.626
4	38	7.04	1.15	3.061	.488	3.755	.578
5	36	6.73	1.23	3.066	.599	3.577	.620
KIDNEYS combined-Male							
1	32	2.78	0.35	.829	.111	1.345	.177
2	43	2.75	0.32	.840	.112	1.338	.169
3	47	2.74	0.31	.825	.090	1.333	.154
4	41	2.84	0.34	.860	.113	1.393	.162
5	36	2.85	0.26	.880	.111	1.383	146
KIDNEYS combined-Female							
1	40	1.89	0.14	.813	.066	1.012	.081
2	37	1.95	0.13	.844	.095	1.037	.071
3	37	1.98	0.20	.871*	.108	1.064	.107
4	38	1.94	0.16	.843	.061	1.034	.088
5	36	2.07*	0.30*	.945*	.195	1.099*	.161
PITUITARY Male							
1	32	.022	.023	.0067	.0076	.0106	.0114
2	43	.016	.006	.0048	.0016	.0077	.0027
3	47	.024	.026	.0074	.0076	.0119*	.0124
4	41	.028	.066	.0092	.0252	.0139	.0351
5	36	.018	.015	.0055	.0045	.0086	.0075

TABLE- 7 CONT.

PITUITARY Female							
1	40	.016	.010	.0069	.0039	.0086	.0053
2	37	.023	.026	.0103	.0141	.0120	.0134
3	37	.040*	.071	.0180*	.0321	.0220*	.0386
4	38	.021	.033	.0087	.0121	.0112	.0177
5	36	.033*	.052	.0157*	.0278	.0176*	.0280
BRAIN $\bar{w}$ STEM Male							
1	32	2.07	.06	.618	.041		
2	43	2.06	.06	.629	.033		
3	47	2.06	.07	.620	.042		
4	41	2.04	.08	.618	.052		
5	36	2.07	.11	.638	.062		
BRAIN w STEM Female							
1	40	1.87	.06	.805	.063		
2	37	1.88	.06	.816	.088		
3	37	1.86	.08	.820	.082		
4	38	1.87	.06	.818	.068		
5	36	1.88	.06	.857*	.077*		
OVARIES							
1	39	.108	.039	.0467	.0176	.0582	.0215
2	36	.105	.040	.0456	.0184	.0560	.0215
3	37	.125	.067	.0538	.0247	.0670	.0354
4	38	.115	.034	.0504	.0168	.0612	.0184
5	36	.131	.060	.0589*	.0260	.0693	.0320
THYROID/PARATHYROID Male							
1	32	.027	.009	.0082	.0027	.0133	.0043
2	41	.031	.009	.0094	.0029	.0150	.0046
3	46	.032	.011	.0097	.0034	.0157	.0054
4	41	.033*	.007	.0100*	.0020	.0163*	.0036
5	36	.034	.014	.0106*	.0041	.0166	.0063
THYROID/PARATHYROID Female							
1	40	.025	.006	.0106	.0028	.0131	.0033
2	37	.024	.007	.0105	.0037	.0128	.0038
3	37	.027	.005	.0117	.0023	.0143	.0027
4	38	.031*	.008	.0134*	.0035	.0164*	.0044
5	35	.027	.009	.0123	.0042	.0144	.0048

b. Gross Pathology

Inspection of detailed gross necropsy findings revealed that there were no differences in incidence of the findings between the control and treated animals with unscheduled deaths, at the 52 week sacrifice, or at the terminal sacrifice.

c. Microscopic Pathology

1) Non-neoplastic

52-Week Sacrifice

There were general alterations in histopathological parameters in the kidneys of groups 3, 4, and 5 that appeared compound-related. These consisted of:

1) An increased incidence in brown tubular cell pigment in the males of groups 3, 4 and 5 (9/10, 10/10, 10/10 respectively) and groups 3, 4 and 5 females (5/10, 6/10 and 7/10 respectively) when compared to control males (2/10) and control females (3/10).(Note appended page 14 for details)

2) An increased frequency and severity of fine vacuolization of cytoplasm in the renal cortex in group 5 females (8/10) when compared to control females (5/10) and an increase in severity in groups 3 & 4 females when compared with control females. (see appended page 14 for details on increased severity.)

Unscheduled Deaths

No compound-related histopathologic alterations were found in the animals that died or were killed moribund prior to the terminal sacrifice.

Terminal Sacrifice

Compound-induced histomorphologic alterations occurred in the kidneys of groups 3, 4 and 5 males and females. (These are summarized on table 8.)

These were:

1) Increased brown tubular cell pigment in the kidneys of groups 3, 4 and 5 males (8/47, 18/41**, 18/36** respectively) and groups 3, 4 and 5 females (23/37*, 19/38**, 13/36 respectively) when compared to control males (2/32) and females (8/40).(Note appended page 15 for statistical analysis)

2) Increased incidence of pelvic microcalculi in groups 4 and 5 males (8/41, 9/36 respectively) and group 5 females (28/36**) when compared to control males (2/32) and female (19/40).

3) A slight increase in frequency of transitional epithelial hyperplasia in group 5 females (6/36) when compared to controls (0/40) however, the study pathologists considered this secondary to the increased frequency of microcalculi.

TABLE 8

NON-NEOPLASTIC LESIONS IN RATS FED 2,4-D

Tubular Cell Pigment, increased kidney	Males					Females				
	1	2	3	4	5	1	2	3	4	5
UD*	0	1	1	0	1	0	1	0	1	2
IS**	2	2	9	10	10	3	3	5	6	7
TS***	2	0	8	18	18	8	9	23	19	13
Total	4	3	18	28	29	11	13	28	26	22
Transitional Epithelial Hyperplasia										
US	0	0	0	0	3	1	1	0	2	5
IS	0	0	0	0	0	2	1	1	3	3
TS	0	1	1	1	0	0	0	3	2	6
Total	0	1	1	1	3	3	2	4	7	14
Microcalculi Pelvis										
UD	0	0	1	0	2	0	2	1	2	7
IS	0	1	0	0	1	2	3	1	3	4
TS	2	2	3	8	9	19	9	14	21	28
Total	2	3	4	8	12	21	14	16	26	39
Fine cytoplasmic Vacuolization										
UD	0	0	0	0	0	0	0	0	0	0
IS	0	0	0	0	0	5	3	5	5	8
TS	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	5	3	5	5	8

*UD = unscheduled deaths
**IS = Interim sacrifice
***TS = Terminal sacrifice

2) Neoplastic

Astrocytomas were found in the brains of rats with unscheduled deaths and terminal sacrifice, including a group 1 male that died in week 21 and two group 4 males that were killed in extremis in week 94 and 105, and one group 5 male that was killed in extremis in week 93. There were no reported astrocytomas found in the 52-week interim sacrifice but at the 104-week terminal sacrifice, 5 astrocytomas were found in group 5 males and none in the other four groups. The total astrocytomas found for male rats on test then totaled 1/60 for group 1 controls, with 0/60, 0/60, 2/58 and 6/60 for groups 2,3,4 and 5 respectively. .(See appended

pages 17,18 and 19 for summary tables and individual animal data). According to the study text,"The incidence of astrocytomas in the brain of high-dose males is higher than that in control males, intercurrent mortality adjusted prevalence analysis indicates a positive trend at p = 0.0026 (one-tailed, uncorrected score test), and control versus high-dose group comparison is significant at p = 0.0351 (one-tail); but not at two-tail (p = 0.0702). (See appended page 20 for statistical analysis).

D. DISCUSSION:

comments:

1. The administration of 2,4-D appears to produce astrocytomas in brains of male rats at 45 mg/kg/day dose level, and is suggestive of a carcinogenic effect. The task force that submitted the study for EPA review is presently re-reviewing the diagnoses of the brain slides and will submit another independent pathology report some time in July, 1986. This task force should be asked to submit summary tables for the urinalysis data and compile concise summary incidence tables for all the non-neoplastic and neoplastic histopathology data. They should also be requested to furnish EPA with all control and treated brain and spinal cord slides for our own independent analysis.

2. Based on the increase in frequency and/or severity of kidney lesions seen in groups 3, 4 and 5 male and female rats the NOEL for non-neoplastic lesions is 1 mg/kg/day, the LEL = 5 mg/kg/day.

TS-769:VAN GEMERT:6/25/86

cc. W. Burnam
T. Farber
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J. Melone
J. Lamb
J. Moore

Pages 15-34 Access to FIFRA health and safety data is restricted under FIFRA section 10(g)

SAMPLE SHEET

EVERY PATHOLOGY REPORT SHOULD HAVE INDIVIDUAL:
HISTOPATHOLOGY INCIDENCE TABLE

005234

Male Mice
Scheduled Sacrifices

Group 1

ANIMAL NUMBER	168-456	168-457	168-458	168-459	168-460	168-461	168-462	168-463	168-464	168-465	168-466	168-467	168-468	168-469	168-470	168-471	168-472	168-473	168-4
LUNG		X				X	X				X			X	X		X	X	X
Alveolar/Bronchiolar Carcinoma																			
Malignant Lymphoma																			
Malignant Lymphoma, Undifferentiated																			
Alveolar/Bronchiolar Adenoma								p		p									
Carcinoma, Metastatic																			
Granulocytic Leukemia																			
Sarcoma, Metastatic					p														
Multifocal Pleuritis																			
Multifocal Pneumonitis			2																
Alveolar Macrophages, Pigmented																1			
Focal Alveolar/Bronchiolar Hyperplasia																			
Congestion																			
Focal Hemorrhage								3											
Alveolar Macrophages																			
Foci of Foamy Macrophages																			
Leukocytosis																			
Peribronchial/Vascular Mononuclear Cells	1		1	1							2	1				1			
Alveolar Proteinosis																			
Multifocal Alveolar-Bronchiolitis	1															1			

SAMPLE SHEET

EVERY PATHOLOGY REPORT SHOULD HAVE:
SUMMARY INCIDENCE TABLE

emale Mice

	Group 1			Group 5			Group 6			Group 7		
	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total	Scheduled Sacrifice	Moribund Sacrifice & Death	Total
UNG (NO. EXAMINED)	(43)	(7)	(50)	(42)	(8)	(50)	(38)	(12)	(50)	(39)	(11)	(5
Alveolar/Bronchiolar Carcinoma	2		2	2		2	2		2	3		3
Malignant Lymphoma					1	1		4	4		1	1
Malignant Lymphoma, Undifferentiated		2	2				1		1		1	1
Alveolar/Bronchiolar Adenoma	3		3	3		3	5	2	7	4		4
Carcinoma, Metastatic	1	1	2		1	1		2	2			
Granulocytic Leukemia					1	1						
Sarcoma, Metastatic												
Multifocal Pleuritis							1		1	3		3
Multifocal Pneumonitis	5		5	2		2	4		4	3		3
Alveolar Macrophages, Pigmented	7		7	4		4				1	1	2
Focal Alveolar/Bronchiolar Hyperplasia	2		2	2		2	2		2	1		1
Congestion	2	2	4	4	5	9	3	5	8	3	8	1
Focal Hemorrhage				2		2	1		1	1		1
Alveolar Macrophages	2		2	2		2	2		2	1		1
Foci of Foamy Macrophages	4		4	3		3				2		2
Leukocytosis				1	2	3					3	3

END